UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/521,958 | 01/21/2005 | Hiroyuki Shirai | TOYA129.008APC | 2101 |

20595 7590 04/09/2008

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER | |
|---|---|
| JEAN-LOUIS, SAMIRA JM | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 04/09/2008 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/521,958 | SHIRAI ET AL. | |
| | Examiner | Art Unit | |
| | SAMIRA JEAN-LOUIS | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Amendment*

This Office Action is in response to the amendment submitted on 01/16/08. Claims 1 and 3 are pending in the applications, with claim 2 having being cancelled. Accordingly, claims 1 and 3 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Regarding the priority of the instant application, receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d) for foreign priority based on an application filed in Japan on July 29, 2002, which papers have been placed of record in the file.

Applicant's argument with respect to Kimura teaching an oil component of only 3% resulting in a phase separation in the Declaration under 37 CFR 1.132 has been considered but is not found persuasive. While example 3 teaches the inclusion of 3% oil, Kimura also teaches 20% adipic acid oil as well (see pg. 5, example 2). As a result, it would have been obvious to the skilled artisan to utilize at least 20% of the oil component along with the disclosed ingredients (including a surfactant) which would result in no phase separation as Kimura and the instant application teach the same exact ingredients in their preparation.

Applicant's contention in the Declaration under 37 CFR 1.132 that the surfactant must possess a melting point of 40 °C or higher is not found persuasive because Kimura discloses the exact same surfactant as the instant application which signifies that the compound would necessarily possess the same physical properties. Moreover, applicant is reminded that a prior art reference may render obvious without disclosing a feature of the claimed invention, as long as that missing characteristic is necessarily present, or inherent, in the anticipating reference. Please see *Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991).* Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. *Please see, e.g., In re Cruciferous Sprout Litig, 301 F.3d 1343, 1351 (Fed. Circ. 2002); MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1366 (Fed. Cir. 1999)* (Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results". In the instant case, the unappreciated "no phase separation" does not require recognition by Kimura.

Applicant's argument that Kimura et al. does not teach a gel/cream formulation is acknowledged but is not found persuasive. Specifically, Kimura et al. teaches the composition as a liquid medicine, cream, ointment, gel, pasting agent, and an aerosol agent (see 3, paragraph 0007.

Applicant's contention that the Sigma Aldrich reference does not teach polyethylene glycol monostearate with a melting point of 40 °C or higher is acknowledged and is found persuasive. However, Kimura et al teaches the exact same surfactant as the instant application (i.e. polyethylene glycol monostearate) signifying that the compound would necessarily possess the same physical properties. Thus, given that these characteristics are physical properties of the compound (i.e. melting point) and such property is inseparable from the parent compound, it would have been obvious to one ordinary to one of ordinary skill at the time of the invention that the surfactant of Kimura et al. would necessarily possess a 40 °C melting point as it is the same exact compound as that of applicant.

Applicant's argument that that the composition of Kimura et al. is sticky and unpleasant due to a low oil concentration and that the oil and polyethylene glycol monostearate are included merely for dissolution purposes is acknowledged and is found non-persuasive. Kimura et al. teaches the exact same surfactant as the instant application (i.e. polyethylene glycol monostearate) and at least 20% oil in his composition, therefore such composition would necessarily possess the same desirable characteristics as the instant application. Moreover, given that the claims are directed to a composition the intended use of Kimura et al. for the oil and the polyethylene glycol is immaterial as they both teach a composition, therefore the intended use is not afforded patentable weight.

In view of applicant's amendment, the 102 (b) rejection is withdrawn in light of applicant's argument, however, the merits of the primary reference will be discussed

since Kimura et al. is retained and the following 103 (a) Non-Final rejections are being made.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**Claims 1 and 3 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Kimura et al. (JP 10-182458, previously cited).**

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Kimura et al. teaches an indomethacin-containing composition comprising 0.1-2% indomethacin in the composition (see pg. 1, paragraph 3 and pg. 3, paragraph 005). Kimura et al. further teaches that the composition can be formulated as a cream, gel, ointment, liquid medicine, pasting agent or aerosol agent (see pg. 3, paragraph 0007). Moreover, several solvents can be added to the composition including water, and lower alcohol (i.e. methanol, ethanol, isopropyl alcohol, etc...), solubilizing agents (i.e. oil of adipic acids, polyethylene glycols, etc...), wetting agents such as propylene glycol, glycerin, etc...) and additional ingredients such as medium chain-fatty acid triglyceride, fatty acid ester, surface acting agents (i.e. sorbitan fatty acid ester (i.e. instant claim 2 since sorbitan fatty acid ester necessarily reads on sorbitan monostearate), glycerine fatty acid ester), polyoxyethylene glycol fatty acid ester, and gelling agents (see pg. 4, paragraph 008). Kimura further exemplify a gel preparation containing indomethacin, 0.01 polyethylene glycol monosterate, 5.0% of an oil component, 0.5% carboxyvinyl polymer (i.e. gelling agent), 30% alcohol, and water of up to 51.5% (without adding the % of indomethacin) based on the amount of the other ingredients (instant claim 1; see pg. 5, example 3). Kimura et al. further teaches that his composition overcomes the prior art since his composition offers better stimulus (i.e. enhanced penetration of the drug) and minimal side effects (see pg. 2, paragraphs 003-0004 and pg. 6, paragraph 0017).

Kimura et al. does not specifically teach an oil component in the amount of 7-30% or water in an amount 20-50% in his composition.

Kimura et al., however, teaches that at least 20% of adipic acid oil can be added to his composition (see pg. 5, working example 2 for adipic oil concentration). Additionally, Kimura et al. teaches the use of water of up 51.5% based on the amount of ingredients added (see pg. 5, paragraph 0013).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize at least 20% oil in the composition of Kimura et al. since Kimura et al. teaches at least 20% oil in his cream compositions. Similarly, to one of ordinary skill in the art at the time of the invention would have found it obvious to vary the water content in the gel or cream composition of Kimura et al. depending on the amount of indomethacin being used in the composition. Given that Kimura et al. teaches an indomethacin-containing composition entailing alcohol, gelling agent, oil, water, and polyethylene glycol monostearate in his composition, one of ordinary skill would have been motivated to vary the water content and utilize at least 20% oil in the composition of Kimura et al. with the reasonable expectation of providing a cream composition with enhanced drug content and absorption and a composition that produces minimal adverse effects.

**Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inagi et al. (4,309,414).**

Inagi et al. teaches a gelled ointment comprising indomethacin, a medium consisting of a glycol, alcohol, water, and a gelling agent selected from cellulose and

carboxyvinyl polymers (see abstract and col. 2, lines 9-11). Additionally, adjuvants can be incorporated into the composition including diisopryl adipate (i.e., oil component; col. 2, lines 14-16). Suitable solvents include glycols such as polyethylene glycol in an amount ranging from 5-35%, alcohols such as ethanol, isopropanol in 10-50%, and water in an amount ranging from 30-55% (see col. 2, lines 24-29). Carboxyvinyl polymer can be used as the gelling agent in a final concentration of 0.5-5% (see col. 2 lines 32-41). Adjuvants such as diisopropyl adipate can be added in a final concentration of 0.5-5% along with Indomethacin in a concentration of 0.5-1.5% (see col. 2, 42-49). Inagi et al. further exemplifies the composition in example 4 which contains 1% carboxyvinyl polymer, 1% Indomethacin, 10% polyethylene glycol 300 (also known as polyethylene glycol 300 monostearate), 30% ethanol, 2% diisopropyl adipate, and about 54.1% of water.

Inagi et al. does not specifically teach 7-10% oil in its composition or water in the amount ranging from 20-50%.

Inagi et al., however, teaches the use of 30-55% water which is in overlapping in scope with the instant application. Moreover, Inagi et al. teaches the addition of adjuvants (i.e. oil) to increase absorption of indomethacin (see col.2, lines 14-16). Thus, it would have been well within the purview of the artisan to vary the 2% concentration of oil and increase it to 7-10% for higher indomethacin absorption.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to vary the concentration of water since Inagi et al. teaches a water

concentration from 30 to 55%. Similarly, one of ordinary skill in the art at the time of the invention would have found it obvious to vary the concentration of oils to 7-10% since Inagi et al. teaches that adding such adjuvants can lead to increased absorption of indomethacin. Given that Inagi et al. teaches an indomethacin composition with alcohol, water, and a gelling agent, and given that Inagi et al. teaches the addition of adjuvants in his composition, one of ordinary skill would have been motivated to vary the concentration of oil given the disclosure of Inagi et al. with the reasonable expectation of providing a gelled ointment composition containing at least 7% diisopropyl adipate with enhanced indomethacin absorption.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

04/01/2008

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617